UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,096	02/01/2001	Dan Nilsson	54337.000009	6906

21967 7590 10/09/2003

HUNTON & WILLIAMS
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1652	22

DATE MAILED: 10/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,096	NILSSON ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-17,24 and 26-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-17,24 and 26-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 23, 2003, has been entered.

[2] Claims 1-7, 9-17, 24, and 26-32 are pending.

[3] Applicant's arguments filed in Paper Nos. 18 and 21 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

[5] At page 9, applicant states, "[a]pplicants continue to traverse the assertion of the lack of unity of invention". However, applicant fails to present any arguments pointing out the supposed errors in the restriction requirement. Furthermore, the lack of unity has previously been made FINAL (see item 1 of Paper No. 17). As applicant presents no

argument addressing the lack of unity and in view of applicant's cancellation of claims 18-23, the traversal is rendered moot.

Claim Objections

[6] In view of applicant's amendment to claim 24 and cancellation of claim 25, the objection to claims 24-25 is withdrawn.

[7] Claim 26 is objected to as blanks appear before parts (i), (ii), and (iii) of the claim. It is suggested that applicant remove the blanks from the claim.

Claim Rejections - 35 USC § 112, Second Paragraph

[8] In view of applicant's amendment to claim 1 to delete the phrase "whereby the bacterial culture is not susceptible to attack by bacteriophages", the rejection is withdrawn.

[9] Claims 1-7, 9-17, 24, and 26-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 1 (claims 2-7, 9-17, 28, 29, and 32 dependent therefrom), 26, 27, and 31 are indefinite in the recitation of "modifying" or "metabolically modifying" as it is unclear as to what modification(s) of milk by the bacterial strain or modified lactic acid bacterium is/are intended by applicant. It is noted that the specification discloses the term "modifying a substrate material" as "[relating] to any aerobic or anaerobic breakdown of organic compounds by a bacterial culture

with the production of an end product" (page 6, lines 3-54 of the specification). However, this broad definition fails to provide a clear meaning of the term "modifying" and as such, the meaning of the term remains unclear.

[b] Claim 9 (claim 32 dependent therefrom) is indefinite in the recitation of "including *E. coli*". A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, the claim recites the broad recitation "*Enterobacteriaceae*", and the claim also recites "*E. coli*" which is the narrower statement of the range/limitation.

[c] Claim 24 recites the limitation "said substrate material". There is insufficient antecedent basis for this limitation in the claim.

[d] Claim 30 is indefinite in the recitation of "susceptibility to attack by bacteriophages". It is noted that an example of the term "not susceptible to attack by bacteriophages" is provided in the specification (page 6, lines 10-11). However, the meaning of the term remains unclear and it is suggested that applicant clarify the meaning of the term. See also item 4 of Paper No.17.

Claim Rejections - 35 USC § 112, First Paragraph

[10] Claims 1-3, 6-7, 9-17, 24, 26-27, and 30-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of modifying milk using a bacterial culture which is capable of being metabolically active in said milk but is not capable of DNA replication, RNA transcription, or protein synthesis or a modified lactic acid bacterium and if the milk is contaminated with a bacteriophage, the metabolic activity of the bacterial culture or lactic acid bacterium is substantially unaffected by the bacteriophage.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only two representative species of the genus of recited bacterial cultures or modified lactic acid bacterium, i.e., a purine (Pur-) or thymidine (*thyA)* auxotrophic bacterium. The

specification fails to describe any additional representative species of the recited genus of bacterial cultures. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the recited genus of bacterial cultures encompasses widely variant species having any modification that results in the bacteria being incapable of DNA replication, RNA transcription, or protein synthesis, wherein the metabolic activity of the bacterial culture on milk is substantially unaffected by bacteriophage contamination. Thus, the genus of recited bacterial cultures is widely variant in both structure and function. As such, the disclosure of the two representative species of bacterial cultures is insufficient to be representative of the attributes and features of *all* species encompassed by the recited genus. Given the lack of description of a representative number of bacterial cultures, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

It is noted that applicant's arguments addressing the instant rejection in amendments filed April 08, 2003 and July 23, 2003 appear to be identical. Therefore, the examiner will refer only to applicant's argument in the amendment of July 23, 2003. At page 10 of the amendment of July 23, 2003, applicant argues the specification provides written description of bacterial strains that can be used to practice the claimed invention and cites alleged supporting text for such disclosure. Applicant argues that the

specification, including the disclosure of specific species, provides a clear indication that applicant possessed the claimed invention at the time of filing. Applicant points out that the invention is directed to a method of modifying milk and not a method of producing auxotrophic bacterial strains. Applicant's argument is not found persuasive.

After reviewing applicant's alleged support for "a number of specific species" of bacterial cultures as recited in claim 1, the examiner can locate only two representative species of the recited bacterial cultures as described above. These two representative species fail to represent the entire genus of recited bacterial cultures. While the examiner acknowledges that the claims are directed to a method of modifying milk, it is noted that the recited genus of auxotrophic bacterial strains are a necessary element of the claimed invention. MPEP § 2163 states, "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art". In this case, there is no evidence of record to suggest that the entire genus of recited auxotrophic bacterial strains with the ability to modify milk even in the presence of bacteriophage contamination were known in the art. Thus, the two auxotrophic bacterial strains disclosed in the specification fail to be representative of the entire recited genus. It is noted that applicant has presented the reference of Morishita et al. (*J Bacteriol* 148:64-71; cited in the IDS filed July 23, 2003) that discloses auxotrophic Lactobacili, which are defective in an amino acid biosynthetic pathway and require amino acid supplementation in order to survive. However, there is no indication in the reference of Morishita et al. the instant specification, or any other

prior art of record that would indicate that these auxotrophic Lactobacili have the ability of being incapable of DNA replication, RNA transcription or protein synthesis in milk whose metabolic activity is unaffected by the presence of bacteriophage. It is noted that claim 1 provides the limitation that the bacterial strain "is not capable of DNA replication, RNA transcription or protein synthesis" in milk. Due to the presence of various amino acids in milk, the auxotrophic strains as described by Morishita et al. would be capable of replication, transcription, and translation as the milk would provide the necessary amino acids to supplement the growth of the strains. This is in contrast to the *thyA* and Pur- mutant representative bacterial stains disclosed in the specification which are incapable of growth in milk because milk contains insufficient amounts of purine and pyrimidine nucleotides to support the growth of purine or pyrimidine auxotrophs of lactic acid bacteria (see Dickley et al. US Patent 5,691,185, columns 11 and 30).

[11] Claims 1-7, 9-17, 24, and 26-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of acidifying milk using a purine or pyrimidine auxotrophic bacterial culture, does not reasonably provide enablement for a method of performing *any* modification of milk using *any* bacterial culture which is capable of being metabolically active in said milk but is not capable of DNA replication, RNA transcription, or protein synthesis or *any* modified lactic acid bacterium and if the milk is contaminated with a bacteriophage, the metabolic activity of the bacterial culture or modified lactic acid bacterium is substantially unaffected by the bacteriophage. The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass a method of performing *any* modification to milk using *any* bacterial culture which is capable of being metabolically active in said milk but is not capable of DNA replication, RNA transcription, or protein synthesis or *any* modified lactic acid bacterium and if the milk is contaminated with a bacteriophage, the metabolic activity of the bacterial culture or modified lactic acid bacterium is substantially unaffected by the bacteriophage. The broad scope of the claimed methods are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of bacterial cultures and lactic acid bacteria broadly encompassed by the claims. In this case the

disclosure is limited to a method of acidifying milk using a purine or pyrimidine auxotrophic bacterial culture.

- The lack of guidance and working examples: The specification provides only two working examples of the recited bacterial culture or modified lactic acid bacterium, i.e., a *Lactococcus lactis* Pur- mutant (see, e.g., page 9, lines 9-16 of the specification) and a *Lactococcus lactis thyA* mutant (see, e.g., page 9, lines 18-25 of the specification), which are capable of acidifying milk. These two working examples fail to provide the necessary guidance for making the entire scope of claimed methods. While it is noted that the specification provides methods for mutating a bacterium (see, e.g., page 8 of the specification), such guidance is insufficient to provide the necessary guidance that would enable a skilled artisan to make all bacterial cultures and modified lactic acid bacterium as broadly encompassed by the claims. In this case, the specification merely provides a starting point for additional research providing no more than a plan or invitation for those of skill in the art to experiment in order to generate the entire scope of recited bacterial cultures or modified lactic acid bacteria. See *University of Rochester v. G.D. Searle & Co. Inc.,* W.D. N.Y., No. 00-CV-6161L, 3/5/03.

- The high degree of unpredictability in the art: While methods for generating mutant bacterial strains are well known in the art, it is highly unpredictable as to whether such methods will generate bacteria having the ability to perform *any* modification to milk. This is particularly true in view of the lack of guidance provided in the specification as discussed in detail above.

- The amount of experimentation required is undue: In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicant argues (beginning at the bottom of page 10 of the amendment filed July 23, 2003) the specification provides sufficient guidance to enable a skilled artisan to make the entire scope of claimed methods. Applicant argues the invention is not directed to making auxotrophic bacterial strains, but is instead directed to the use of auxotrophic strains for modifying milk even in the presence of bacteriophage contamination. Applicant submits the reference of Morishita et al. (*J Bacteriol* 148:64-71; cited in the IDS filed July 23, 2003) to support an assertion that "it was well known for the person skilled in the art, at the time of the present invention, how to provide auxotrophic mutants of lactic acid bacteria" particularly lactic acid bacteria "showing

auxotrophic behavior against different amino acids, vitamins and other nutrients". Applicant argues they have allegedly discovered that auxotrophic bacteria whose ability to replicate DNA, transcribe RNA, or synthesize protein is attenuated, the bacteria nonetheless is capable of acidifying milk. Applicant argues that the Pur- and *thyA* mutants shown in the specification should only be viewed as illustrative and the scope of the claims should not be limited to these working examples. Applicant's argument is not found persuasive.

As stated in detail above, the specification fails to enable the entire scope of bacterial strains and modified lactic acid bacteria. In particular, the specification merely provides a starting point for additional research providing no more than a plan or invitation for those of skill in the art to experiment in order to generate the entire scope of recited bacterial cultures or modified lactic acid bacteria. See *University of Rochester v. G.D. Searle & Co. Inc.,* W.D. N.Y., No. 00-CV-6161L, 3/5/03. The examiner acknowledges that the invention is not directed to making auxotrophic bacterial strains, but is instead directed to the use of auxotrophic strains for modifying milk even in the presence of bacteriophage contamination. However, this does not preclude the specification from teaching how to make the broad scope of auxotrophic bacterial strains that can be used in the claimed method. It is noted that there is evidence of record that would suggest that *any* auxotrophic bacterial strain will be useful for practicing the invention. For example, the *Lactococcus lactis* Pur- mutant and *Lactococcus lactis thyA* mutant as disclosed in the specification are shown to be incapable of replicating DNA, transcribing RNA, or synthesizing protein in milk as milk

has been shown to contain insufficient amounts of purine and pyrimidine nucleotides to support the growth of purine or pyrimidine auxotrophs of lactic acid bacteria (see Dickley et al. US Patent 5,691,185, columns 11 and 30). However, the auxotrophic strains as described by Morishita et al. would appear to be capable of replication, transcription, and translation as the milk would provide the necessary amino acids to supplement the growth of the strains. As applicant has provided no evidence of record that the auxotrophic strains of Morishita et al. would have the desired characteristics as recited in the claims and the auxotrophic strains of Morishita et al. would not be useful for practicing the claimed invention. Furthermore, even if such evidence were presented, the claims are not so limited to the auxotrophs disclosed in the specification (Pur- and *thyA* mutants) or the strains as disclosed by Morishita et al.

[12] It is noted that the deposit requirement under 35 USC 112, first paragraph for claims 28 and 29 has been satisfied in view of applicant's submission of Declarations of Deposit filed November 145, 2002 as Paper No. 16.

Conclusion

[13] Status of the claims:

- Claims 1-7, 9-17, 24, and 26-32 are pending.
- Claims 1-7, 9-17, 24, and 26-32 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be

reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

10/02/03

DAVID STEADMAN
PATENT EXAMINER